

Appl. No. : 10/552,881
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AMENDMENTS TO THE CLAIMS

1-35. (Canceled)

36. (Currently amended) A process for producing a cross-linked polysaccharide gel comprising:

(a) contacting a polysaccharide mixed in an alkaline medium with a bifunctional or polyfunctional epoxide cross-linker to provide an essentially ~~epoxy~~ cross-linked polysaccharide wherein the ~~epoxide~~ cross-linker is substantially linked to the polysaccharide by ether bonds;

(b) drying the ~~epoxy~~ cross-linked polysaccharide without substantially removing epoxide from the alkaline medium to form a cross-linked polysaccharide matrix; and

~~(c) optionally washing the cross-linked polysaccharide matrix with a water miscible solvent; and~~

~~(d)~~ (c) neutralising the cross-linked polysaccharide matrix with an acidic medium to form a cross-linked polysaccharide gel.

37. (Previously presented) The process according to claim 36 wherein the polysaccharide is hyaluronic acid, pectin, xanthan or alginic acid.

38. (Currently amended) The process according to claim 36 wherein the polysaccharide is selected from the group consisting of an anionic derivative of carboxymethyl cellulose, carboxymethyl dextran, hyaluronic acid, or carboxymethyl starch and an anionic derivative of carboxymethyl cellulose.

39. (Previously presented) The process according to claim 38 wherein the polysaccharide is hyaluronic acid.

40. (Previously presented) The process according to claim 36 wherein the epoxide is 1,4 -butanediol diglycidyl ether, 1,2-ethanediol diglycidyl ether or an epoxy-substituted pentaerythritol.

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41. **(Previously presented)** The process according to claim 40 wherein the epoxide is 1,4 -butanediol diglycidyl ether.

42. **(Previously presented)** The process according to claim 36 wherein the alkaline medium has a pH in the range of about 9 to 12.

43. **(Previously presented)** The process according to claim 42 wherein the alkaline medium comprises between 1 and 5 wt/vol percent polysaccharide and between 0.05 and 0.5 wt/vol percent epoxide.

44. **(Previously presented)** The process according to claim 43 wherein the epoxide contacts the polysaccharide at a temperature of at least about 45°C.

45. **(Currently amended)** The process according to claim 44 wherein the cross-linked polysaccharide matrix is dried under vacuum at a temperature of at least about 35°C.

46. **(Currently amended)** The process according to claim 36 wherein steps (a) to (e) and (b) are performed under alkaline conditions.

47. **(Currently amended)** The process according to claim 46 67 wherein the optional washing step (e) ~~further~~ comprises washing the cross-linked polysaccharide matrix with acetone.

48. **(Previously presented)** The process according to claim 47 wherein the neutralisation step (d) further comprises freeze drying the cross-linked polysaccharide gel and reconstituting the gel.

49. **(Previously presented)** The process according to claim 48 wherein the freeze dried cross-linked polysaccharide gel is reconstituted in phosphate buffered saline.

50. **(Previously presented)** The process according to claim 49 further comprising combining the polysaccharide with a biologically active substance.

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51. **(Withdrawn)** A cross-linked polysaccharide gel substantially resistant to hyaluronidase degradation prepared by the process according to claim 36.

52. **(Withdrawn)** The gel according to claim 51 wherein the gel releases less than about 75 percent uronic acid under hyaluronidase treatment.

53. **(Withdrawn)** The gel according to claim 51 wherein the gel releases no more than about 70 percent uronic acid under hyaluronidase treatment.

54. **(Withdrawn)** The gel according to claim 51 wherein the gel releases no more than about 65 percent uronic acid under hyaluronidase treatment.

55. **(Withdrawn)** The gel according to claim 51 wherein the gel releases less than about 75 percent uronic acid after being extruded or expelled from a 32 gauge needle.

56. **(Withdrawn)** The gel according to claim 51 wherein the gel releases no more than about 70 percent uronic acid after being extruded or expelled from a 30 gauge needle.

57. **(Withdrawn)** The gel according to claim 51 further comprising a biologically active substance.

58. **(Withdrawn)** The gel according to claim 57 wherein the biologically active substance is a hormone, cytokine, vaccine, cell, tissue augmenting substance, or mixture thereof.

59. **(Withdrawn)** The gel according to claim 58 wherein the tissue augmenting substance is collagen, starch, dextranomer, polylactide, poly-beta-hydroxybutyrate, or copolymers thereof.

60. **(Withdrawn)** The gel according to claim 57 wherein the biologically active substance is an alkaloid, peptide, phenothiazine, benzodiazepine, thioxanthene, hormone, vitamin, anticonvulsant, antipsychotic, antiemetic, anesthetic, hypnotic, anorexigenic, tranquilizer, muscle relaxant, coronary vasodilator, antineoplastic, antibiotic, antibacterial, antiviral, antimalarial, carbonic anhydrase inhibitor, nonsteroid antiinflammatory agent,

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vasoconstrictor, cholinergic agonist, cholinergic antagonist, adrenergic agonist, adrenergic antagonist narcotic antagonist or combination thereof.

61. **(Withdrawn)** A pharmaceutical composition comprising:
a cross-linked polysaccharide gel substantially resistant to hyaluronidase degradation prepared by the process according to claim 36;
a biologically active substance; and
a pharmaceutically acceptable carrier.
62. **(Withdrawn)** The pharmaceutical composition according to claim 61 wherein the preparation is in the form of a pill, tablet, capsule, suppository, spray, cream ointment or sticking plaster.
63. **(Withdrawn)** A method of treating or preventing a disorder or condition selected from the group consisting of tissue augmentation, arthritis, tissue adhesions, immunogenicity, diseases of the mucosa, dermatological conditions, ophthalmological conditions, hormonal conditions, joint lubrication conditions and cosmetic conditions, in a subject in need thereof, comprising administering a therapeutically effective amount of a gel substantially resistant to hyaluronidase degradation prepared by the process according to claim 36.
64. **(Withdrawn)** The method according to claim 63 wherein the gel further comprises a biologically active substance, and a pharmaceutically acceptable carrier.
65. **(Withdrawn)** The method according to claim 63, wherein the administration to the subject is by injection.
66. **(Withdrawn)** The method according to claim 63, wherein the administration to the subject is by topical application.
67. **(New)** The process according to claim 36, further comprising , between steps (b) and (c), washing the cross-linked polysaccharide matrix with a water miscible solvent.

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68. (New) The process according to claim 67, wherein the washing step is performed under alkaline conditions.

69. (New) The process according to claim 36, wherein the cross-linked polysaccharide gel is substantially resistant to hyaluronidase degradation.